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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/027,205	02/20/98	JUNE	C GIN-005

000959
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HM12/1009

EXAMINER	
ROARK, J	
ART UNIT	**PAPER NUMBER**
1644	19

DATE MAILED: 10/09/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/027,205	Applicant(s) JUNE ET AL.	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,55,60,75 and 87-94* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,55,60,75 and 87-94* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 8/9/01 (Paper No. 18), is acknowledged.
Claims 56-59, 61-74 and 76-86 have been cancelled. Claims 2-54 have been cancelled previously.
Claims 87-94 have been added.
Claims 1, 55, 60 and 75 have been amended.
Claims 1, 55, 60, 75 and 87-94 are pending and are under consideration in the instant application.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 8/9/01 (Paper No. 18).
The rejections of record can be found in the previous Office Action (Paper No. 16).

It is noted that New Grounds of Rejection are set forth herein.

3. Applicant's cancellation of Claims 56-59, 61-74 and 76-86 have obviated the previous objections and rejections with respect to Claims 56-59, 61-74 and 76-86.

4. Applicant's amendment, filed 8/9/01 has obviated the previous rejection of claims 1, 55, 60 and 75 under 35 U.S.C. 112, first paragraph, as lacking enablement for compounds comprising a CD28 ligand, or for anti-CD28 in the absence of anti-CD3.

5. Claim 91 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method comprising *in vivo* use of a solid phase surface that is a bead, does not reasonably provide enablement for a method comprising *in vivo* use of a solid phase surface that is a plate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

One of skill in the art would not reasonably expect that a solid phase surface that is a tissue culture plate could be employed in *in vivo* methods, nor does Applicant provide guidance or working examples as to how a tissue culture plate cold be employed in the instant method *in vivo*.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, it is unpredictable as to how the skilled artisan could use a tissue culture plate in an in vivo setting. Thus the experimentation left to those skilled in the art to practice the invention is unnecessarily, and improperly, extensive and undue.

6. Applicant's arguments, filed 8/9/01, have been found convincing. The previous rejection of claims 1, 55, 60 and 75 under 35 U.S.C. 112, second paragraph, is withdrawn.

7. Applicant's comments, filed 8/9/01, with respect to In re Katz are acknowledged. However, until such time as the appropriate declaration is filed under 37 CFR 1.132:

Claims 1, 55 and newly added claims 87-90, 92 and 94 are rejected under 35 U.S.C. 102(a) as being anticipated by Levine et al. (Science 272:1939-1942 1996, IDS #CH, see entire document).

Levine et al. teach a method comprising contacting T cells with a solid phase surface comprising an anti-CD3 antibody and an anti-CD28 antibody *in vitro* (see entire document). Both anti-human CD3 and anti-human CD28 antibodies are taught (e.g., page 1939, middle column – OKT3 and mAb9.3 are "anti-human" as evidenced by their reactivity with human T cells). Levine et al. also teach a magnetic immunobead as the solid phase surface and direct immobilization via a covalent modification (e.g., legend of Figure 1).

Although downregulation of an HIV-1 fusion co-factor such as CCR5 is not explicitly demonstrated, the use of identical methodology as that disclosed in the specification as-filed indicates that downregulation of the HIV-1 fusion co-factor CCR5 would be inherent, as evidenced by the resistance of the T cells to infection with the M-tropic (CCR5-dependent) HIV-1 strain.

When a claim recites using an old composition or structure (e.g. a solid phase surface comprising an anti-CD3 antibody and an anti-CD28 antibody) and the use is directed to a result or property of that composition or structure (downregulation of the HIV-1 fusion co-factor CCR5), then the claim is anticipated. See MPEP 2112.02. Also, see Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

It is noted that the CAFC recently held in Bristol-Myers Squibb Co. v. Ben Venue Laboratories Inc., 58 USPQ2d 1508 (CA FC 2001) that the preamble language in claims is an expression of purpose and intended result, and as such is non-limiting, since the language *does not result in a manipulative difference in the steps of the claims*.

Applicant is reminded that the courts have held that there is no requirement that those of ordinary skill in the art know of the inherent property. See MPEP 2131.01(d) and MPEP 2112 - 2113 for case law on inherency.

The rejection is maintained.

8. Claims 1, 55, 60, 75, and newly added claims 87-89, 92 and 94 are rejected under 35 U.S.C. 102(e) as being anticipated by Chang (US Pat. No. 6,129,916, see entire document).

Applicant's arguments, filed 8/9/01, have been fully considered, but are not found convincing, essentially for the reasons of record.

Applicant's arguments are addressed below in the context of the reiterated rejection as applied to the newly added claims.

Chang teaches and claims a method comprising contacting T cells with a microbead coupled with a plurality of binding molecules specific for an antigen on a human T cell, wherein the binding molecules are an antibody to CD3 and an antibody to CD28 (see entire document, especially claims 1-2 and columns 11-12). Chang et al. teach and claim an *in vivo* method, but the use of a microbead coupled with a plurality of binding molecules specific for an antigen on a human T cell, wherein the binding molecules are an antibody to CD3 and an antibody to CD28 *in vitro* is also taught (e.g., column 5, especially lines 31-37). Chang et al. teach several methods for immobilizing antibodies on solid phase surfaces such as beads, including direct immobilization via a covalent modification (see especially columns 7-8).

Although downregulation of HIV-1 fusion co-factors including CCR5 is not explicitly demonstrated, the use of *in vivo* methodology equivalent to that disclosed in the specification as-filed for *in vitro* experiments indicates that downregulation of CCR5 would be an inherent outcome of these methods.

Applicant argues that there is no motivation for the ordinarily skilled artisan to select the particular anti-CD3 plus anti-CD28 combination recited in the instant claims, based upon the teachings of Chang et al. that anti-CD3 and "anti-CD2, anti-CD4, anti-CD5, anti-CD8, anti-CD28 or other binding molecules specific for T cells" can be conjugated to a microbead (column 12 at lines 7-13).

However, a reference that clearly names the claimed species anticipates the claim no matter how many other species are named. It was noted in Ex parte A that when the species is clearly named, the species claim is anticipated no matter how many other species are additionally named. Ex parte A, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990) (MPEP 2131.02).

Applicant also points to column 5 at lines 32-36 and further argues that Chang only teaches that the conjugates can be used in *in vitro* methods diagnostically, such as in standard lymphocyte proliferation assays.

However, it is again noted that when a claim recites using an old composition or structure (e.g. a solid phase surface comprising an anti-CD3 antibody and an anti-CD28 antibody) and the use is directed to a result or property of that composition or structure (downregulation of the HIV-1 fusion co-factor CCR5), then the claim is anticipated. See MPEP 2112.02. Also, see Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

It is noted that the CAFC recently held in Bristol-Myers Squibb Co. v. Ben Venue Laboratories Inc., 58 USPQ2d 1508 (CA FC 2001) that the preamble language in claims is an expression of purpose and intended result, and as such is non-limiting, since the language *does not result in a manipulative difference in the steps of the claims*.

The rejection is maintained.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1, 55, 60, 75, 91 and 93 are rejected under 35 U.S.C. 103(a) as being unpatentable over *either* Levine et al. (Science 272:1939-1942 1996, IDS #CH) *or* Chang (US Pat. No. 6,129,916), each in view of the well-known and art-recognized use of avidin-biotin complexes to couple antibodies to solid phase surfaces, including tissue culture dishes, as evidenced by Shattil (US Pat No. 5,561,047).

The claims are drawn to a method comprising contacting T cells with a solid phase surface that is a tissue culture dish comprising anti-CD28 antibody and anti-CD3 antibody, and to a solid phase surface comprising anti-CD28 antibody and anti-CD3 antibody immobilized via an avidin-biotin complex.

Levine et al. and Chang each have been discussed supra and teach a method comprising contacting T cells with a solid phase surface comprising anti-CD28 antibody and anti-CD3 antibody, wherein downregulation of expression of the HIV fusion cofactor CCR5 is an expected outcome of the method.

Neither Levine et al. nor Chang teach immobilizing antibodies on the solid phase surface via an avidin-biotin complex, not that the solid phase surface may be a tissue culture dish.

However, Chang does teach that any of a variety of methods well known in the art at the time the invention was made can be used to link an antibody to a microbead (see entire document, especially columns 7-8).

Further, it was well known in the art at the time the invention was made that a method of immobilizing an antibody on a solid phase surface included formation of a avidin-biotin complex to link the antibody to the surface. For example, Shattil teaches that a biotinylated antibody (PAC-1) can be immobilized on a support material such as a microtiter well coated with the avidin derivative streptavidin (see entire document, especially column 3 at lines 55 onward). Shattil also teaches that streptavidin coated plates are advantageous in that they can be prepared in advance and stored for long periods before use (e.g., bridging sentence of columns 3 and 4).

While it is noted that one of ordinary skill in the art would not be motivated to utilize a solid phase surface that is a tissue culture dish for *in vivo* methods; for *in vitro* methods one of ordinary skill in the art would expect that beads and plates could be used interchangeably and would function equivalently as a solid phase surface for immobilizing antibodies. Likewise, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute any of a number of methods of immobilizing antibodies of interest on a solid phase surface, including via an avidin-biotin complex. Methods of forming biotin-avidin complexes were well known in the art at the time the invention was made, as evidenced by Shattil; therefore the ordinary artisan would have had a reasonable expectation of success in immobilizing an antibody using this method. The ordinary artisan would have been motivated to utilize the biotin-avidin system because, as evidenced by Shattil; the method was well known in the art at the time the invention was made and offered the advantage of preparing the antibody-coated surface in advance. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

11. No claim is allowed.

12. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica H. Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday, 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
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October 4, 2001

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